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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/035,091

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Holly Hogrefe

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Agilent Technologies, Inc. in care of:  
CPA Global  
P. O. Box 52050  
Minneapolis, MN 55402

EXAMINER

HUTSON, RICHARD G

ART UNIT

PAPER NUMBER

1652

NOTIFICATION DATE

DELIVERY MODE

04/22/2011

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPOPS.LEGAL@agilent.com  
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<b>Office Action Summary</b>	<b>Application No.</b> 10/035,091	<b>Applicant(s)</b> HOGREFE ET AL.	
	<b>Examiner</b> RICHARD HUTSON	<b>Art Unit</b> 1652	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 2/8/2011.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3,10-12,14,20,22-24,26,30,31 and 33-52 is/are pending in the application.
- 4a) Of the above claim(s) 23,24,26,30,31 and 33-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3,10-12,14,20,22,36-52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicant's amendment of claims 1, 10, 12, 22, 31, 33, 36, 37, 36, 40, 41, 44, 45, 48-50 and the addition of new claim 52, in the paper of 2/8/2011, is acknowledged.

Claims 1, 3, 10-12, 14, 20, 22, 23, 24, 26, 30, 31, 33-52 are pending and at issue.

Applicants arguments presented in the paper of 2/8/2011, are acknowledged and have been considered herein.

Claims 23, 24, 26, 30, 31 and 33-35 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 10-12, 14, 20, 22, 36-51 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, 12, 36, 40, 44, 48, 49, 50, (3, 10-11, 14, 20, 22, 37-39, 41-43, 45-47 and 51 dependent from) are indefinite in that the recitation "said second enzyme is the wild type Pfu DNA polymerase comprising the amino acid sequence of SEQ ID NO. 12, except that it is mutated at an amino acid position selected from the group consisting of: Y410, D543, K593, G387, G388, and the following amino acid substitutions: Y385N, Y385W, Y385L, Y385H, Y385Q, and Y385S". This recitation appears to indicate that applicants claimed enzyme mixture comprises a polymerase which is mutated at a

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substitution, suggesting that the polymerase is mutated by substitution and additionally by a second mutation on top of the substitution.

Claim 52 is rejected on the basis that the recitation "the wild type Pfu DNA polymerase comprising the amino acid sequence of SEQ ID NO. 12, except that it is mutated at an amino acid position selected from the group consisting of: T542 and Y5895, or comprises a Y385F mutation" is confusing and unclear. The basis of this is two fold. First reference to a Y5895 amino acid position is unclear. Second, reference to a Y385F mutation is unclear. Is it applicants intent to refer to a "Y385F substitution or a mutation of a "Y385F" in which the mutation is to the substituted residue.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 10-12, 14, 20, 22, 36-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to previous claims 1, 3, 10-12, 14, 20, 22, 36-51. in response to this rejection applicants have amended claims 1, 10, 12, 22, 31, 33, 36, 37, 36, 40, 41, 44, 45, 48-50, added new claim 52 and traverse the rejection as it applies to the newly amended claims.

Applicants continue to traverse the rejection as previous. Applicants continue to submit that Table 1 provides support for the claimed enzymes having both reduced polymerization activity and reduced exonuclease activity as applicants submit that in that Table, nineteen specific mutant enzymes are disclosed that have the claimed characteristic of reduced 3'-5' exonuclease activity and reduced 5'-3' DNA polymerization activity as compared to the wild type Pfu DNA polymerase. With regard to this applicants, while applicants point out that nineteen specific mutant enzymes are disclosed with reduced 3'-5' exonuclease activity, and reduced 5'-3' DNA polymerization activity, at least 6 had equal to or greater than 3'-5' exonuclease activity. Thus Table I does not support applicants claim to this specific sub genus of polymerase mutants

Applicant's continued comments regarding support for this amendment are acknowledged, however, not found persuasive, as applicant's specification clearly does not support that applicants had possession of the newly claimed invention at the time of filing. It continues for example, applicants point to specification at page 20, lines 17-19 which states:

Preferably, the genetic modification for preparing  $\text{exo}^+$  DNA polymerase with reduced polymerization activity does not significantly reduces its 3'-5' exonuclease activity (i.e., the proofreading activity).

While those polymerases with "reduced" 3'-5' exonuclease activity" may be encompassed by the above, clearly applicants invention at the time of invention was not specifically directed to those which had reduced 3'-5' exonuclease activity". Similarly applicant's specification at page 49-50 does not remedy support for such. Thus

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applicant's newly amended claims are drawn to new matter that was not supported by applicant's specification at the time of filing.

Further applicants newly claimed subject matter in which applicants claim those enzyme mixtures in which the polymerase is mutated at a amino acid substitution (i.e. T385N) is not supported by applicants specification at the time of filing and thus considered new matter (See above rejection under 112 second paragraph).

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 10-12, 14, 20, 22 and 36-51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 82-92, 96, 98-102, 116-119, 121, 123-138, 155-158, 163-170, of copending Application No. 10/227,110. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed enzyme mixtures of the instant application, comprising a first enzyme and a second enzyme wherein said first

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enzyme comprises a DNA polymerization activity and said second enzyme is a mutant Pfu DNA polymerase having a mutation at an amino acid position selected from the group consisting of D405, Y410, T542, K593, Y595, Y385, Y387, and G388 and those further limited claims dependent thereon are obvious over the corresponding claims of copending Application No. 10/227,110, drawn to a enzyme mixture comprising a first enzyme and a second enzyme, wherein said first enzyme comprises 5'-3' polymerization activity of a DNA polymerase or reverse transcriptase, and said second enzyme is a mutant of a wild type DNA polymerase, said wild type DNA polymerase comprising the partitioning domain sequence YXGG (SEQ ID NO:6), the polymerase domain sequence DXXSLYP (SEQ ID NO: 1) or DFRALYP (SEQ ID NO: 13), the polymerase domain sequence YXDTDS (SEQ ID NO:4), YIDTDG (SEQ ID NO:15), YADTDG (SEQ ID NO:16), or YSDDTDG (SEQ ID NO: 17), and the polymerase domain sequence KXY, and wherein said second enzyme comprises an amino acid substitution at an amino acid position corresponding to G387 of SEQ ID NO: 19, and wherein said second enzyme comprises 3'-5' exonuclease activity and reduced 5'-3' DNA polymerization activity as compared to the wild type DNA polymerase. Application 10/227,110 further teaches the above enzyme mixtures wherein said mutant polymerase additionally comprises a mutation selected from Y410, T542, K593, Y595, Y385, Y387, and G388, thus making the instant claims obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants request to keep this rejection in abeyance until the time of identification of otherwise allowable subject matter is acknowledged.

It is further acknowledged that application number 10/227,110 will issue as U.S. Patent No. 7,932,070 on 4/26/2011.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.



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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mondesi Robert can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rg  
4/15/2011

/Richard G Hutson/  
Primary Examiner, Art Unit 1652